Delivering genomic medicine in the UK National Health Service: a systematic review and narrative synthesis

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Abstract

Purpose

We sought to assess the readiness of the United Kingdom National Health Service to implement a Genomic Medicine Service. We conducted a systematic literature review aimed to identify what is known about factors related to the implementation of genomic medicine in routine health care and to draw out the implications for the UK and other settings.

Methods

Relevant studies were identified in Web of Science and PubMed from their date of inception to April 2018. The review included primary research studies using quantitative, qualitative or mixed methods, and systematic reviews. A narrative synthesis was conducted.

Results

Fifty-five studies met our inclusion criteria. The majority of studies reviewed were conducted in the US. We identified four domains: 1) systems; 2) training and workforce needs; 3) professional attitudes and values; and 4) the role of patients and the public.

Conclusion

Mainstreaming genomic medicine into routine clinical practice requires actions at each level of the health care system. Our synthesis emphasised the organisational, social and cultural implications of reforming practice, highlighting that demonstration of clinical utility and cost effectiveness, attending to the compatibility of genomic medicine with clinical principles and involving and engaging patients are key to successful implementation.

Keywords: clinical implementation, genomic medicine, personalised care, clinical genetics, service delivery

Introduction

Globally, health systems anticipate the incorporation of genomic medicine into clinical practice. In the United Kingdom, the Genomic Medicine Service was launched in 2018, coinciding with the completion of the 100,000 Genomes Project. The service plans to mainstream genomic testing in the National Health Service (NHS), from single gene to genome sequencing (GS), and, in the long term, expand the use of genomics beyond rare diseases and cancer.[1] This vision was set out in the Chief Medical Officer's 2017 report *Generation Genome* which envisaged the imminent implementation of genomic medicine while acknowledging a need to consider infrastructural, workforce, ethical and other issues raised by an expansion of this technology.[2] Integrating genomic medicine poses considerable challenges to health care organisations, however evidence to support implementation remains lacking[3]. This review aims to identify what is known about factors related to the implementation of genomic medicine in routine health care and to draw out the key implications for the UK and other settings. We conducted a narrative synthesis to examine the complex organisational, social and cultural factors involved in implementing genomic medicine.

Materials and methods

Literature search strategy

We conducted a systematic search for studies that described implementing genomics and genetics into clinical practice. Clinical applications of genomic medicine remain in the early stages; accordingly, our search included clinical genetics to examine the implications of this evidence for genomic medicine. Searches were conducted across two databases, Web of Science and PubMed, and included all literature in the databases from their date of inception to April 2018 (Figure 1). The search strategy combined “genomics” or "genomic medicine" with terms such as “implementation” and “health services” (Supplementary Table S1).

Study selection criteria

The review included primary research studies and systematic reviews. The search was not limited to UK studies, or to countries with similar healthcare systems, as we believed research findings from other settings might be instructive for the UK context. Articles were excluded if they were not written in English. Editorials, commentaries, conference abstracts, and methodological papers without presentation of research findings were excluded. Also excluded were papers with a molecular/biological focus, on peri- or pre-natal genetics, and about genetics research rather than clinical practice. Additional papers were identified through hand-searching reference lists and citation tracking of included studies. After removing duplicates two authors (C.P., E.G.) independently screened the titles and abstracts of identified articles against the eligibility criteria. Cases of disagreement were resolved between the two reviewers; remaining uncertainties were resolved in consultation with C.M. Both reviewers then screened the full texts of the articles. Three authors (C.P., E.G., C.M.) determined the final inclusion.

Data extraction and analysis

A data extraction form was used that included bibliographic information (including country, setting, year of publication), study design and methods, participant characteristics and main findings (Supplementary Table S2). Two authors (C.P., E.G.) independently completed the data extraction for each study which was checked for accuracy and completeness by C.M.

A narrative synthesis was conducted, following the framework established by the Economic and Social Research Council (ESRC).[4] The ESRC framework consists of (1) developing a theory or hypothesis, (2) preliminary synthesis of findings of included studies, (3) exploration of relationships within and between studies, and (4) assessment of the robustness of the synthesis. This approach aims to produce a textual, narrative understanding of findings and synthesise conceptual themes. Narrative synthesis was considered appropriate as we aimed to identify implementation factors across a broad body of evidence that included studies conducted in different settings and with quantitative, qualitative and mixed designs. Two authors (C.P., E.G.) used tabulation and thematic analysis to extract and synthesise data from included studies, using the data extraction summaries and referring to the full text papers. Similarities and differences were then explored across the studies, key domains were identified, and patterns and relationships were grouped into themes. Themes identified by the synthesis were refined until consensus among all authors was reached.

Quality assessment

We assessed the quality of papers using a checklist which scores papers out of five[5] (see Supplementary Table S3). We did not exclude papers with a lower quality score but used the scores to provide one indicator of the robustness of the synthesis.

Results

Study characteristics

A total of 55 papers met the inclusion criteria (Supplementary Table S4). Most studies (n=27) were from the United States (US), with the remaining from the United Kingdom (UK) (n=10), Canada (n=4), The Netherlands (n=2), Estonia (n=1), South Korea (n=1) and Cuba (n=1). One study was conducted across the US and Canada. Studies focused on genetics and/or genomics, including genetic testing (targeted or panel tests), genetic counselling, genome and exome sequencing, and pharmacogenomics.

The studies were either: 'interventional' or 'observational'. Interventional studies implemented and evaluated novel interventions into clinical practice; these included genetics/genomics education for clinicians; demonstrating the effectiveness or feasibility of care models; and testing digital tools. Observational studies examined aspects of clinical practice; these included perceptions and knowledge of genetics/genomics among clinicians and patients; analysing routine data, for example referral rates to genetic services; and surveying health service organisation. Both used a range of methods, including pre/post design, randomised controlled trials, surveys, observation, semi-structured interviews, and statistical data analysis. Study participants were largely non-genetics health professionals, but also genetics counsellors, patients, members of the public, and research participants.

Domains

The narrative synthesis of the literature identified four domains: 1) systems; 2) training and workforce; 3) professional attitudes and values; and 4) the role of patients and the public.

Systems

Service organisation

Five papers described service organisation, identifying inequity and variability in provision, and lack of co-ordination between genetics and non-genetics services.[6–10] Two reviews of specialised services in the UK found variation in referral and genetic testing rates between regions,[6] and an inverse relationship between referrals and deprivation.[7]

Variability was also reported in a survey of the US Veterans Health Administration (VHA) genetics services.[8] Services were largely delivered through multidisciplinary clinics or coordinated services, but this was not consistent. For some clinicians, genetics services were only available at different clinical sites, via telemedicine, or at non-VHA facilities.

Clinicians in the US and UK reported lack of service co-ordination as a barrier to integrating genetics services.[9,10] In UK general practice, staff attitudes reflected institutional arrangements and commissioning decisions that regarded genetics as 'specialist' and 'peripheral' to mainstream services.[10]

Digital systems

Eight papers described the use of digital systems, evaluating clinical decision support (CDS) tools and investigating the ability of electronic health records (EHRs) to organise genetic information.[11–19] The development of interoperable digital systems and data storage facilities has been identified as central to mainstreaming genomic medicine in the NHS.[20] Studies we identified described challenges to implementing digital systems.

Six evaluated digital decision support.[11–16] Digital reminders increased family history documentation and referral rates for patients in two studies.[11,12] Two studies evaluated pharmacogenomics CDS.[13,14] One found that clinicians considered the alerts helpful for prescribing decisions[13]; the other reported that clinicians found alerts confusing and frustrating and had little impact on prescribing decisions.[14] Barriers to implementing pharmacogenomics CDS were reported across eleven clinical sites, however these were found to be caused by general IT problems, and not specific to genomic medicine.[15] A systematic review of digital CDS for genetics concluded that further research is needed to understand how CDS can be integrated with current systems.[16]

Three studies described challenges when using EHRs to organise genetic or genomic data, suggesting that current systems were not ready to meet the future demands of genomic medicine.[17-19] Few US-based clinicians (genetics and non-genetics specialists) and EHR representatives (including chief/executive medical officers, product managers, and information technology (IT) specialists) felt EHRs met their current genomic medicine needs.[17] Respondents stated the need for structured and standardised data elements such as: functions to order genetic tests; results organised and displayed in pedigree format; and the ability to interpret familial risk. This finding was reflected in a US study of genetic test reporting in EHRs: no standard reporting format was used by the laboratories. EHRs were described as serving as storage for textual reports rather than meaningful structured data.[18] Sperber et al.[19] identified integrating genomics into EHRs as a challenge for US service providers, however using data warehousing techniques was found to aid integration across organisations.

Policies and guidelines

Seven papers described the impact of policies and guidelines on integrating genomics/genetics into practice.[10,21–26]

Clinicians reported a lack of guidelines for: pharmacogenomics testing,[21] the collection of family health history,[22] and the disclosure of secondary findings.[23] Lack of guidelines was cited by clinicians as a barrier to genetics service integration, but it could not be determined whether this finding resulted from an actual lack or lack of clinician awareness.[24]

Two studies described difficulties translating policies or guidelines into practice.[25,26] In the UK, clinical genetics guidelines conceptualise genetic information as confidential to families rather than individuals. Despite this, UK-based clinicians reported that decision-making around confidentiality and disclosure remained based on an individual model.[25] A US study examining the impact of an insurance-mandated requirement for genetic counselling prior to testing for *BRCA1* and *BRCA2* found that, contrary to the policy's purpose, a higher number of people did not complete genetic testing after policy introduction.[26]

Changes to health service funding impacted on the delivery of genetic services in the UK, leading to the discontinuation of pilot genetics services in general practice[10] and a low prevalence of follow up appointments, preventing familial communication about genetic information.[25] Responsibility for the governance and allocation of funding for UK genetic services was also reported as 'ambiguous.'[10]

Access

Five studies described patient access to genetics services.[27–31] Clinic or hospital location, along with patient ability to pay and health insurance coverage, were more frequently cited as barriers to genetic counselling by US-based genetics professionals (genetic counsellors and genetics service providers) than patient attitudes, norms and education.[27,28] Though social factors, such as discouragement by family members, were also identified.[28]

Changing clinic location facilitated access in two studies.[29,30] Delivering genetic counselling in primary care (general practice) compared with secondary care (hospital) led to higher rates of referral and attendance in a UK-based trial.[29] In a US study, telemedicine enabled access to genetics services by saving patients' time and travel costs.[30]

A systematic review of factors acting as barriers to patient referral to genetics services found that few studies focused on access. The evidence examined did not differentiate between access to referrals and the utilisation of services.[31]

Health service costs

Four papers analysed the organisational costs of genomic medicine.[24,29,32,33]

Two examined the cost-effectiveness of GS.[32,33] A systematic review found that the current health economic evidence base to support use of genome and exome sequencing is limited and called for more studies evaluating costs and cost-effectiveness.[32] A cost analysis of a randomised control trial (RCT) delivering GS in US primary care found that short-term costs were driven primarily by the costs of sequencing, interpretation, and disclosure, but did not find evidence that GS increased downstream costs such as health-care utilisation.[33]

Two papers investigated the costs of integrating genetics services.[24,29] Clinicians perceived costs of unreimbursed time spent counselling and ordering tests as a barrier to integration.[24] However, clinic costs (measured by staff travel and transportation) were not increased by delivering genetic counsellor appointments in UK general practice compared with tertiary/secondary care.[29]

Training and workforce needs

Clinician preparedness

Twenty papers describing the preparedness of clinicians[9,14,21-24,28,31,34–46] found some variations across specialities, but overall clinicians lacked knowledge and/or confidence to implement genomic medicine into practice.[9,21,22,34] Reports described little direct experience with using genetic services[22,35,36]; feeling unprepared to order tests[21,37]; interpret and disclose results[9,22,38] and secondary findings[23]; use pharmacogenomics information[14]; and respond to patient queries about direct-to-consumer testing.[39]

Clinicians' lack of knowledge and awareness could act as a barrier to patients accessing and being referred to genetic services,[31] such as genetic counselling.[28,41] Shields et al.[42] found reduced utilisation of genetic tests and referrals among US clinicians who served populations with higher proportions of ethnic minority groups, but it was unclear whether the finding was due to clinician training or reflected the populations' different needs.

A lack of comprehensive genetics/genomics training was identified in two surveys, of clinicians in Canada[21] and medical course directors in the US and Canada.[40] Most clinicians reported that they had not received graduate or postgraduate training in pharmacogenomics or genetics.[21] Course directors agreed that medical training was insufficient preparation for using genetics/genomics in clinical practice.[40]

Differences were identified in the knowledge and skills across nongenetic specialities.[9,21,35,38] A survey of US clinicians found that, depending on specialty, respondents had different expectations of the skills required. Areas such as neurology and oncology were expected to be more skilled in genetic risk assessment, testing, and management compared with cardiology and primary care.[35]

Limited experience with genetic and genomic information among the primary care workforce (family physicians and general practitioners) was highlighted in three studies.[34,44,45] Study respondents expressed discomfort with discussing inheritance patterns; the contribution of genetics to common, complex disease; and communicating potential risk to family members.[44] Lacking direct clinical experience, they reported that personal experiences, such as the experiences of family and friends, influenced their attitudes toward and perceptions of genomic medicine.[34] This lack of knowledge was cited as a barrier to the integration of genetic services in two systematic reviews.[24,43]

However, primary care clinicians did report feeling comfortable talking to patients about basic genetics and taking a family history[44]; demonstrated an understanding of direct-to-consumer reports[45]; and the ability to manage and make appropriate clinical recommendations from GS results.[46]

Genomics/genetics education

Seven papers investigated educational interventions for clinicians, including six evaluations of novel education interventions[11,29,47–50] and one systematic review.[51] The studies reported that education interventions improved genetics knowledge amongst clinicians. One reported an increase in referral rates to genetics services.[29] The systematic review found insufficient evidence to inform future educational interventions and recommended interventions should be assessed by changes in practice, such as patient management, rather than knowledge and confidence of clinicians.[51]

Genetics/genomics specialists

The role of genetics or genomics specialists was described in eight papers.[8,22,24,30,31,34,52,53] Five[8,22,24,31,32] reported that clinicians had variable or limited access to genetics services and reported having 'unfamiliar' relationships with geneticists.[32] The lack of genetics expertise across the workforce was identified as a barrier to patient referral to genetic services in a systematic review.[31]

Three described use of multi-disciplinary teams (MDTs) to deliver specialised genetics services.[30,52,53] Evaluation of an American paediatric telemedicine service demonstrated a positive impact on patients who reported high satisfaction, especially in underserved areas, because of the model's flexibility and decrease in waiting times.[30] Members of a rare disease MDT in the UK described how they valued the clinical and scientific diversity to make informed decisions about eligibility for GS, though it was acknowledged the MDT was resource intensive and, beyond certain conditions, remains unusual in UK health services.[52] A pre/post study evaluating MDTs to treat inherited retinal dystrophy found that the model was delivered consistently but it was not clear what impact the MDT had on the overall outcomes of the study.[53]

Professional attitudes and values

Clinician attitudes

Nine papers investigated clinicians' attitudes to genomic medicine, demonstrating that clinicians held positive beliefs about the potential of genomic medicine.[9,22,23,35–38,44,54] However, several risks were identified, including, misinterpretation of results by clinicians[23] or patients[44]; clinician errors in ordering genetic tests[54]; and fear of causing patients unnecessary stress[44] or harm.[54] One study highlighted the potential risks of disclosing secondary findings, asserting that clinicians need to consider not only clinical utility but psychosocial, ethical, and legal factors.[23]

Five described clinician concerns about the clinical utility, defined as evidence of improving prediction, treatment and management of disease and enabling clinical decision making, and applicability of genomic medicine.[9,22,35,37,54] Some concerns related specifically to mainstream use of GS.[23,38] The added value of genetic testing, compared with existing practice, for predicting disease or treatment outcomes was also viewed as ambiguous by clinicians across five specialties in a US-based study.[35]

Compatibility with current practice and values

Fifteen papers highlighted the level of compatibility of genetics or genomic medicine to current practice and values.[9,10,22–25,35-38,52,55-58] Four used ‘diffusion of innovation’ theory[59] to assess how certain attributes, including compatibility with organisational and individual values, norms, and needs, influenced adoption into routine use.[22,35,36,58]

In terms of practice, clinicians expressed concerns about the impact on workload and workflow,[9,37] specifically a lack of time to order tests or explain results,[24,36] and, for some clinicians, the complex logistics involved in ordering and receiving approval for genetic tests.[35]

Clinician views on compatibility varied according to type of test; overall, genetic testing was judged on clinical utility, in terms of whether use could inform clinical management and decision making.[35,58] This included consideration of the patient population and the condition. Genetic testing for colorectal cancer was perceived as of low need by clinicians working in one organisation due to the older patient age served by the provider.[22] In a US survey, most clinicians agreed that predictive testing for conditions where there is no available treatment, such as Huntington's, was compatible with professional and personal beliefs.[36]

Compatibility with professional role was perceived differently across specialties. Clinicians and staff working in general practice, family or internal medicine did not feel delivering genetics services was part of their role, or were unclear about their role in providing genetics services,[9,10,24] and tended to view genomic medicine as complex compared with those working in specialisms such as gynecology and paedatrics.[36]

Compatibility also included consideration of health organisation/provider values. The US Veteran's Heath Administration viewed the mainstreaming of genetic services as incompatible with system values of low cost and high clinical impact.[35] However, a study from Cuba found genetic services were adopted successfully into national health services, challenging the assumption that a personalised model of care is a prerequisite to the expansion and translation of genomics.[55]

Issues around confidentiality and secondary findings presented challenges to clinicians' sense of responsibility towards patients in three UK studies.[23,25,57] Clinicians described a struggle to both use a familial approach to confidentiality[25] and act in the patients' best interests, exacerbated by a lack of guidelines and evidence.[23] Interviews with research participants found that decisions to disclose secondary findings need to consider individual patients' tolerance for uncertainty.[57] Research recruitment within healthcare settings also posed challenges for UK health care professionals. Recruitment targets for the 100,000

Genomes project affected decision making over eligibility and suitability for GS[57]; and overshadowed commitments to patient informed consent.[56]

Patients and public

Patient and public involvement has been identified as key to the successful delivery of genomic medicine in the NHS.[2] The knowledge, awareness and engagement of patients and public was described in nine papers.[19,28,29,43,57,60–63] Studies demonstrated that patients and members of the public were aware of and generally held positive attitudes toward genetic testing[61] but were less informed about the role of genes in disease[62] and genetic services available to them.[31,43] This low awareness could act as a barrier to referral to services such as genetic counselling.[28,31]

Patients and research participants often overestimated the potential of genetic testing or GS to provide clinical benefits.[60,63] Engaging and educating patients was identified to address this.[43,60–63] One study[19] recommended specific strategies including, actively involving patients in implementation and decision-making.

Six papers described patient outcomes of genetic/genomic services.[26,29,30,43,46,53] One systematic review reported that genetic/genomic services or interventions for common chronic diseases had modest positive effects on psychological outcomes and mixed behavioral outcomes.[43] Three used patient-reported measures to assess psychological and behavioural outcomes of a specialised genetics service for ophthalmology patients[53]; genetic counselling prior to *BRCA1* and *BRCA2* testing[26]; and healthy patients receiving GS.[46] All three studies demonstrated little significant change in patient-reported outcomes. Participants in the GS trial did report making health behaviour changes related to the results and perceived them as medically useful in terms of influencing their medical treatment.[46] However, some differences were found: the trial participants that received GS results expressed slightly lower levels of satisfaction and confidence with how well they understood the information compared with those that received a family history report only.

Two further studies evaluated patient satisfaction.[29,30] A US telemedicine paediatric clinic seeking to identify nonsyndromic developmental delay reported high satisfaction,[30] while no difference in level of patient satisfaction was found when comparing genetic counselling (for cancer and non-cancer conditions) delivered in general practice or a hospital setting.[29]

Discussion

Genomic medicine is being mainstreamed into routine preventative, diagnostic and interventional health care, bringing challenges for how health care organisations may need to change to deliver this new technology. Our review identifies current knowledge about factors that will enable delivery of genomic medicine, focusing on four categories of interest: systems, training and workforce needs, professional attitudes and values, and the role of patients and the public.

The majority of studies reviewed were conducted in the US. Differences in the governance and financing of US health services means that not all the domains identified will be relevant to the UK. In the US, patient ability to pay and health insurance coverage will factor into access to genetics/genomics services. Equally, prioritising cost-effectiveness may limit NHS patient access to genetics and genomics services. US studies[8,9,15,22,35,58] conducted in the VHA, along with findings from countries with some level of nationally funded health service

- and the domains addressed in these studies - may be more immediately relevant to the UK setting.

However, health systems in these settings operate in contexts of varied economic, political, and social factors. This means that although genomic medicine seeks to transform global health systems, implementation will vary across and within local contexts. Here we draw out implications for the UK, acknowledging important differences that exist between health service structure and organisation, to identify key issues shared across largely western/industrialised contexts.

Through a systematic synthesis of current evidence on genomic medicine implementation across a range of domains, our review provides an overview of the key factors influencing health service readiness. The findings support existing recommendations[63,64] that identify practical challenges at each level of clinical practice, including coordinated infrastructure and a trained and prepared workforce. We also found that the compatibility of professional, patient and system values with genomic medicine plays a key role. This echoes the *Generation Genome* report which states that genomic medicine is as much a 'cultural and political exercise' as a scientific one.[2] Summarising our findings we have, thus, identified three overarching themes: reforming practice (referring to systems, training and workforce); the value of genomic medicine (referring to professional attitudes and values); and revising the 'social contract' (acknowledging the role of patients and public).

Reforming practice

Our review suggests that at least some genetic services are not well integrated into clinical practice, raising questions over service co-ordination and equity of access. Acknowledging the parity of access and 'cottage industry' of NHS genetic services, the *Generation Genome* report outlined intentions to streamline and centralise services, embedding national standards, in preparation for the Genomic Medicine Service. Papers we reviewed highlighted the need for guidelines to aid clinicians in tasks such as ordering genetic tests, making appropriate referrals, and interpreting results.

The need for standardised digital systems was identified, in particular consistent reporting formats and digital decision support tools in EHRs. Developing digital infrastructure in the NHS is a priority, specifically the capacity to store genetic data, linking local sites to a central database, and integrating genetic information into EHRs.[20] Our review identified little literature that focused on the interoperability of systems or addressed informatics capabilities for managing GS data. However, findings from genomic research projects have proposed digital solutions and standards, which may in the future translate into clinical practice.[19,65]

Regarding training and workforce needs, in accordance with other systematic reviews, we identified differences in the knowledge and skills of those working in specialisms and those working in primary care (general practice or family medicine).[23,42,66] This was reflected in the attitudes of staff in primary care settings, who regarded genetics as of little relevance to their practice. In current primary care practice, genetics and genomics may feature rarely, however the 'whole NHS' approach proposed by the Genomic Medicine Service indicates that in the medium to long term the skills expected of the UK primary care workforce are likely to change.

Developing genetics/genomics education programmes for nongenetic health professionals has therefore become a priority. The NHS aims to produce a 'genomic literate' workforce, reforming training and education by integrating a new ‘genomic paradigm’ into current medical curricula.[2] The impact of these initiatives will become evident in the long term. Our review demonstrated education programmes had mixed success and the long-term impact remains unclear. This finding indicates the limitations of isolated interventions; multifaceted health interventions have been found to be more likely to improve practice.[67] A systematic review of genetics/genomics education for nongenetic health professionals also highlighted shortcomings in programme design and evaluation.[68] To date there has been a lack of engagement with implementation science frameworks in genomic medicine literature,[3] yet our review identifies that successful education may require a wider re-clarification of roles, norms and values.

Along with training new and existing staff, developing a multi-disciplinary approach to delivering genomic medicine has been prioritised.[20] We found few descriptions of MDTs in practice. Prevalence varies between specialty, and refining our search to a specific condition, such as cancer, may have yielded more results.

The value of genomic medicine

Papers we reviewed emphasised the need for robust evidence of the clinical utility of genomic medicine, that is, evidence that treatments improve patient outcomes and/or enable clinical management. A 2008 review identified a lack of evidence for clinical outcomes, demonstrating the persistence of the problem.[42] The lack of demonstrable clinical utility or benefit raises broader questions about the value of genomic medicine. Vassy et al.[70] argued that the common understanding of clinical utility may need revising to account for genomic medicine. Considering instead the ‘appropriateness’ of a treatment would involve evaluating whether the expected benefits exceed the expected negative consequences. For example, GS could be deemed appropriate if it serves to end the diagnostic odyssey and inform reproductive choices. For certain conditions, a diagnosis could also change clinical outcomes by enabling patients to receive treatment earlier, improving prognosis.

The appropriateness of genomic medicine may then include clinical utility but also the values of professionals and patients. Studies of patient and public attitudes toward genetic testing suggest they are driven by a broader understanding of utility that includes gaining a sense of control over one's health[71] or may experience a moral imperative to undertake testing[72]; similar sentiments may apply to genomics. Review findings indicate patients, the public, and research participants can overestimate the benefits of genetic testing and GS, suggesting a gap between the expectations and reality of what both can provide.

Clinical benefits may include changes in patient behaviour, often cited as a rationale for genomic medicine. Papers we reviewed demonstrated only modest effects. The impact of genetic results on behaviour has been shown to be limited.[73,74] Christensen and Green,[75] drawing on preliminary trial results, speculate that genomic information, specifically secondary findings from GS, could foster health behaviour change unlike typical risk assessments.

Value refers not only to clinical benefits: genomic medicine may help to deliver care that is cost effective and value for money.[4] We found little evidence for cost effectiveness or impact on health service costs, indicating the complexity of estimating and evaluating cost effectiveness and economic benefit. Nevertheless, genomic medicine in the UK is positioned as an investment opportunity that, it is claimed, will create jobs and develop a competitive research environment.

Rethinking the social contract

Mainstreaming genomic medicine, according to the *Generation Genome* report,[4] signals a need to rethink the 'social contract' set out in the NHS constitution, describing how patients, the public, and staff are bound together by shared principles and responsibilities. Rethinking the 'social contract' would involve broadening patient consent and the current 'narrow' model of confidentiality, balancing the interests of patients against those of family members and 'broader society.'

As the 'mainstreaming agenda' is implemented, questions about confidentiality and familial communication are likely to become more pertinent. Review findings suggest that expanding the traditional model of patient-doctor confidentiality may be difficult to implement in practice, and clinicians expressed concerns over patient harm. This difficulty may reflect a disjuncture between the focus on personalised care, of which genomics is considered a central part, and some of the implications of mainstreaming genomic medicine which may force clinicians to reassess their understanding of responsibility.

The NHS vision states that clinicians' duty of care towards patients (and family members) should be extended to researchers, bioinformaticians and data managers. In genetics, it is well acknowledged that the boundaries between care and research are often blurred.[75,76] Genomic medicine heightens issues around secondary findings and patient confidentiality, provoking further concerns around balancing informed consent and clinical benefits, and requiring better efforts to engage and inform the public about genomic data use.

Our review has some limitations. First, it is possible that despite using validated databases relevant articles that were not indexed and/or written in languages other than English were not identified. Second, we used a broad search strategy to capture the range of factors involved in the implementation of genomic medicine. As such, our search returned studies on both genetics and genomics and we have sought to clarify the specificities between the two. Third, while the impact on nongenetic professionals remained our focus, studies involving geneticists/genetic counsellors were included, judged on relevance to routine care. Fourth, although our synthesis focused on the requirements of the NHS to implement genomic medicine, our review draws on mostly non-UK literature and we have sought to address important differences between the health services of the included papers.

Despite these limitations, this systematic review contributes to the clinical genomics and genetics field by highlighting key actions required to implement genomic medicine into routine practice. In particular, our review has highlighted the new obligations and responsibilities that are being demanded of patients, clinicians and health services, demonstrating not only the organisational, but also the social and cultural implications of reforming practice. Following on from the completion of the 100,000 Genomes project, implementation of the NHS Genomic Medicine Service will likely accelerate. The UK provides an example for health services worldwide that seek to implement genomic technologies into routine practice. As such the results of this review may guide future integration of genomic medicine in the UK and globally.

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